

Sub B2 indicates a phenotypic, physiological, behavioural or biochemical change in the nematode worms.

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Sub B3
16. (Amended) A method as claimed in claim 14 [or claim 15] wherein the genetically encoded marker molecule is an autonomous fluorescent protein, alkaline phosphatase, luciferase, β -glucuronidase, β -lactamase, β -galactosidase, acetohydroxyacid synthase, chloramphenicol acetyl transferase, horseradish peroxidase, nopaline synthase, octapine synthase or aequorin.

Sub B4
17. (Amended) A method as claimed in any one of claims 1 to [16] 7 wherein the non-visual detection means is a multi-well plate reader.

Sub B5
19. (Amended) A method as claimed in any one of claims 1 to [16] 7 wherein the non-visual detection means is a FANS device.

Sub B6
21. (Amended) A method as claimed in any one of claims 1 to [9] 7 wherein the step of detecting a signal comprises detecting the size and/or developmental stage of the nematode worms using a FANS device.

Sub B7
23. (Amended) A method as claimed in any one of [the preceding claims] claims 1 to 7 wherein step (a) comprises dispensing substantially equal volumes of a homogeneous suspension of nematode worms into each of the wells of the multi-well assay plate.

Sub B8
27. (Amended) A method as claimed in any one of [the preceding claims] claims 1 to 7 wherein the nematode worms are synchronized in the same growth stage.

Sub B9
29. (Amended) A method as claimed in claim 27 [or claim 28] wherein the worms are hermaphrodites or males.

Sub B10
30. (Amended) A method as claimed in any one of [the preceding claims] claims 1 to 7 wherein the nematode worms are a wild type strain, a mutant strain, a transgenic strain or a humanized strain.

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34. (Amended) A method as claimed [in claim 32] in claim 32 [or claim 33] wherein expression of the toxic gene is driven by a tissue-specific promoter which is capable of directing gene expression in a single tissue, a sub-set of cell types, a single cell type or a single cell of *C. elegans*.

sub 63/10 A
36. (Amended) A method as claimed in any one of [the preceding claims] claims 1 to 7 wherein the method is performed in a liquid assay medium containing a water soluble polymer at a concentration sufficient to increase the viscosity of the medium.

sub C3
39. (Amended) A method as claimed in [any one of claims 36 to 39] claim 36 wherein the concentration of water soluble polymer in the liquid medium is 0.3%.

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40. (Amended) A method as claimed in any one of claims 1 to [35] 7 wherein the method is performed in a liquid assay medium containing a water soluble polymer at a concentration sufficient to prevent the nematode worms from sticking to the wells of the multi-well plate.

sub C3 A12
42. (Amended) A method as claimed in claim 40 [or claim 41] wherein the concentration of water soluble polymer in the liquid medium is from 0.01% to 10%.

sub B13 A13
53. (Amended) A method as claimed in any one of claims 44 to [52] 50 wherein the step of detecting changes in the pharynx pumping rate comprises contacting the nematode worms with a marker molecule which generates a signal when taken up by nematode worms and detecting the said signal using non-visual detection means.

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58. (Amended) A method as claimed in any one of claims 44 to [57] 50 wherein the non-visual detection means is a multi-well plate reader.

sub B15 A15
60. (Amended) A method as claimed in any one of claims 44 to [57] 50 wherein the non-visual detection means is a FANS device.

sub B16 A16
62. (Amended) A method as claimed in any one of claims 44 to [61] 50 wherein said nematode worms are wild-type mutant, transgenic or humanized *C. elegans*.

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67. (Amended) A method as claimed in claim 65 [or claim 66] wherein the transgenic *C. elegans* further carry a mutation in the *C. elegans* gene encoding SERCA protein.

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71. (Amended) A method as claimed [in claimed] in claim 69 [or claim 70] wherein expression of the toxic gene is driven by a tissue-specific promoter which is capable of directing gene expression in the *C. elegans* pharynx, in a sub-set of cells of the *C. elegans* pharynx, in the pharyngeal neurons or in a single pharyngeal neuron.

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73. (Amended) A method as claimed in claim 69 [or claim 70] wherein expression of the transgene is driven by the daf-7 promoter.

74. (Amended) A method as claimed in any one of claims 44 to [73] 50 wherein the nematode worms are synchronized in the same growth stage.

76. (Amended) A method as claimed in claim 74 [or claim 75] wherein the worms are hermaphrodites or males.

77. (Amended) A method as claimed in any one of claims 44 to [76] 50 wherein the method is performed in a liquid assay medium containing a water soluble polymer at a concentration sufficient to increase the viscosity of the medium.

80. (Amended) A method as claimed in [any one of claims 77 to 79] claim 77 wherein the concentration of water soluble polymer in the liquid medium is 0.3%.

81. (Amended) A method as claimed in any one of claims 44 to [76] 50 wherein the method is performed in a liquid assay medium containing a water soluble polymer at a concentration sufficient to prevent the nematode worms from sticking to the wells of the multi-well plate.

83. (Amended) A method as claimed in claim 81 [or claim 82] wherein the concentration of water soluble polymer in the liquid medium is from 0.01% to 10%.

91. (Amended) A method as claimed in any one of claims 86 to [90] 89 wherein the non-visual detection means is a multi-well plate reader.

93. (Amended) A method as claimed in any one of claims 86 to [90] 89 wherein the non-visual detection means is a FANS device.

95. (Amended) A method as claimed in any one of claims 86 to [94] 89 wherein the nematodes are synchronised in the same growth stage.

97. (Amended) A method as claimed in claim 95 [or claim 96] wherein the nematodes are hermaphrodites or males.

107. (Amended) A method as claimed in any one of claims 98 to 104 [106] wherein the step of detecting changes in the movement behaviour of the nematode worms comprises measuring the level of autofluorescence a sub-region of the material in the wells of the multi-well assay plate.

108. (Amended) A method as claimed in any one of claims 98 to 104 [107] wherein the non-visual detection means is a multi-well plate reader.

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A28 110. (Amended) A method as claimed in any one of claims 98 to 104 [109] wherein the nematode worms are synchronized in the same growth stage.

112. (Amended) A method as claimed in claim 110 [or claim 111] wherein the worms are hermaphrodites or males.

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B27 113. (Amended) A method as claimed in any one of claims 98 to 104 [112] wherein the nematode worms are a wild type strain, a mutant strain, a transgenic strain or a humanized strain.

A30 117. (Amended) A method as claimed [in claimed] in claim 115 [or claim 116] wherein expression of the toxic gene is driven by a tissue-specific promoter which is capable of directing gene expression in a single tissue, a sub-set of cell types, a single cell type or a single cell of *C. elegans*.

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A31 119. (Amended) A method as claimed in any one of claims 98 to 104 [118] wherein the method is performed in a liquid assay medium containing a water soluble polymer at a concentration sufficient to increase the viscosity of the medium.

122. (Amended) A method as claimed in claim 119 [any one of claims 119 to 121] wherein the concentration of water soluble polymer in the liquid medium is 0.3%.

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B29
A32 123. (Amended) A method as claimed in any one of claims 98 to 104 [118] wherein the method is performed in a liquid assay medium containing a water soluble polymer at a concentration sufficient to prevent the nematode worms from sticking to the wells of the multi-well plate.

A33 125. (Amended) A method as claimed in claim 123 [or claim 124] wherein the concentration of water soluble polymer in the liquid medium is from 0.01% to 10%.

A34 137. (Amended) A method as claimed in claim 135 [or claim 136] wherein expression of the toxic gene is driven by the her-1 P2 promoter, the mab-18 promoter or the spe-T1 promoter.

A35 149. (Amended) A method as claimed in claim 134 [or claim 145] wherein the transgenic *C. elegans* express a marker molecule.

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A36 151. (Amended) A method as claimed in any one of claims 127 to 131 [150] wherein the step of detecting the amount of eggs or offspring produced comprises adding a
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Sub B32
specific antibody which binds to eggs, L1 stage, L2 stage, L3 stage or L4 stage nematodes and detecting complexes formed by binding of the antibody to eggs, L1 stage, L2 stage, L3 stage or L4 stage nematodes using non-visual detection means.

152. (Amended) A method as claimed in any one of claims 127 to 131 [151] wherein the non-visual detection means is a multi-well plate reader.

A36
153. (Amended) A method as claimed in any one of claims 127 to 131 [150] wherein the step of detecting the amount of eggs or offspring comprises directly counting the numbers of eggs or offspring using a FANS device.

154. (Amended) A method as claimed in any one of claims 127 to 131 [150] wherein the step of detecting the amount of eggs produced comprises detecting the activity an enzyme released from the eggs on hatching.

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156. (Amended) A method as claimed in any one of claims 127 to 131 [155] wherein the method is performed in a liquid assay medium containing a water soluble polymer at a concentration sufficient to increase the viscosity of the medium.

159. (Amended) A method as claimed in claim 156 [any one of claims 156 to 158] wherein the concentration of water soluble polymer in the liquid medium is 0.3%.

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160. (Amended) A method as claimed in any one of claims 127 to 131 [155] wherein the method is performed in a liquid assay medium containing a water soluble polymer at a concentration sufficient to prevent the nematode worms from sticking to the wells of the multi-well plate.

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162. (Amended) A method as claimed in claim 160 [or claim 161] wherein the concentration of water soluble polymer in the liquid medium is from 0.01% to 10%.

Sub B36 A40
179. (Amended) A method as claimed in any one of claims 164 to 177 [178] wherein the method is performed in a liquid assay medium containing a water soluble polymer at a concentration sufficient to increase the viscosity of the medium.

182. (Amended) A method as claimed in claim 179 [any one of claims 179 to 181] wherein the concentration of water soluble polymer in the liquid medium is 0.3%.


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Sub B37
183. (Amended) A method as claimed in any one of claims 164 to 177 [178] wherein the method is performed in a liquid assay medium containing a water soluble polymer at

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a concentration sufficient to prevent the nematode worms from sticking to the wells of the multi-well plate.

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185. (Amended) A method as claimed in claim 183 [or claim 184] wherein the concentration of water soluble polymer in the liquid medium is from 0.01% to 10%.

If any other information is needed, please contact the undersigned attorney by phone (617-720-3500, Ext. 343) to expedite the further prosecution of this patent application.

Respectfully submitted,


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